I. AMENDMENT

Please make the following amendments:

In the Claims:

Please amend claims 19, 30 and 31 as follows:

19. (Amended) A method of producing a virus comprising:

introducing into a host cell a recombinant viral expression construct comprising a polynucleotide encoding a 3' sequence of GBV-B, wherein the polynucleotide comprises 50 contiguous nucleotides from SEQ ID NO:1; and

culturing said host cell under conditions permitting production of virus from said construct.

30. (Amended) The method of claim 19, wherein said polynucleotide comprises recombinant RNA.

31. (Amended) The method of claim 19, wherein said polynucleotide comprises recombinant DNA.

Please add new claim 56 as follows:

--56. (New) A method of producing a virus comprising:

obtaining a virus produced by the method of claim 19,

introducing the virus into a second host cell; and

culturing said host cell under conditions permitting production of virus from said construct.--

These amendments are illustrated in Appendix A attached hereto.

II. RESPONSE TO OFFICE ACTION

Status of the Claims

Claims 19-21, 27-33 and 51-55 were pending prior to the Office Action dated March 27, 2002. Claims 19, 30, and 31 have been amended (Appendix A). Support for the amendments may be found throughout the specification, for example, at least at pages 4-7, 9-13, 31 and 33-37. Thus, no new matter has been added. For the Examiner's convenience, the pending claims are attached hereto as Appendix B.

Claims 51-55 were withdrawn as being non-elected species

The Action contends that claims 51-55 were withdrawn from consideration as being drawn to a non-elected invention since the methods therein are ultimately limited to nucleotides which differ in structure from the nucleotides of the elected methods claims. The Applicants traverse the withdrawal of claims 51-55.

Claims 51-55 depend from claim 19. Claim 19 reads "A method of producing a virus comprising: introducing into a host cell a recombinant viral expression construct comprising a polynucleotide encoding a 3' sequence of GBV-B, wherein the polynucleotide comprises 50 contiguous nucleotides from SEQ ID NO:1; and culturing said host cell under conditions permitting production of virus from said construct." The claim as amended recites SEQ ID NO:1, and claims 51-55 recite SEQ ID NO:2. The Applicants note that SEQ ID NO:2 contains all of SEQ ID NO:1, as shown in the sequence listing and described on page 6 of the specification. Because claims 51-55 incorporate the limitations of claim 19, from which they depend, these claims are directed to nucleic acids whose structure is similar. Hence, no additional search would be required by the Examiner for claims 51-55 should claim 19 be found allowable, because of the overlap in sequence with independent claim 19. The Examiner and the

NO one RNA is true other DNA duplex structure is T.

NO

Applicants' representative discussed in a telephone conference, which Applicants' representative appreciates, the possibility of a species election. Should the Examiner deem a species election between SEQ ID NO:1 and SEQ ID NO:2 to be required, Applicants elect SEQ. ID. NO:1. Applicants retain the right to have a reasonable number of species examined, should the elected species be found patentable.

In light of the foregoing, the Applicants respectfully request that the Examiner reconsider claims 51-55.

Claims 19-21 and 28-30 were rejected based on 35 U.S.C. §101 as being non-statutory

The Action contends that claims 19-21 and 28–30 are rejected under 35 U.S.C. §101 because the invention is directed to non-statutory subject matter. The Applicants traverse this rejection.

Claim 19 recites "A method of producing a virus comprising: introducing into a host cell a recombinant viral expression construct comprising a polynucleotide encoding a 3' sequence of GBV-B, wherein the polynucleotide comprises 50 contiguous nucleotides from SEQ ID NO:1; and culturing said host cell under conditions permitting production of virus from said construct." Because the method involves a "recombinant viral expression construct," which is not found in nature, claim 19 does not encompass naturally occurring virus. Instead, the claim is directed to statutory subject matter. Thus, claim 19, and claims 20-21 and 28-30 which depend from claim 19, is not directed to non-statutory subject matter, but rather statutory subject matter because the steps as outlined in claim 19 would require the intervention of a person.

The Action further contends that the recitation of "synthetic," in claim 30, as a term is meaningless with respect to distinguishing from that which occurs in nature. While the

Applicants dispute this, to expedite prosecution, claim 30 now recites "The method of claim 19, wherein said polynucleotide comprises recombinant DNA."

Thus, in light of the aforementioned, the Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 19-21 and 28-30 under 35 U.S.C. §101.

Claims 19-21 and 27-33 were rejected based on 35 U.S.C. §112 second paragraph

Claims 19-21 and 27-33 are rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps. The Action further contends that the omitted step is: isolating virus from the host cell. The Applicants traverse this rejection and states that there is no essential step omitted and no gaps between the steps.

Claim 19 is directed to a "method of producing a virus." It recites "introducing into a host cell a recombinant viral expression construct comprising a polynucleotide encoding a 3' sequence of GBV-B" and "culturing said host cell under conditions permitting production of virus from said construct." One of ordinary skill in the art would be able to produce a virus by the steps as outlined in claim 19, and described on pages 23-26 and 31-37 of the specification. While it may be advantageous under some circumstances to isolate the virus, it is not essential for practicing the invention—a "method for producing a virus." Accordingly, there is no omitted step in the claimed method.

The Action further contends that the term "comprising a polynucleotide encoding a 3' sequence" in claim 19 renders the claim indefinite. The Action also contends that the specification does not provide a standard for ascertaining the requisite length of the

polynucleotide that one of ordinary skill in the art would be reasonably apprised of the scope of the invention. The Applicants traverse this rejection.

Claim 19 recites "A method of producing a virus comprising: introducing into a host cell a recombinant viral expression construct comprising a polynucleotide encoding a 3' sequence of GBV-B, wherein the polynucleotide comprises 50 contiguous nucleotides from SEQ ID NO:1; and culturing said host cell under conditions permitting production of virus from said construct." The Applicants have provided SEQ. ID.NO:1 and methods of constructing an infectious GBV-B clone, a full length clone and the nucleotide sequence of the cloned GBV-B cDNA, all as provided on pages 33-37 in the Examples of the specifications. One of ordinary skill in the art would be able to determine from the claims what they encompass or exclude, and thus the claims are definite.

Thus, in light of the aforementioned the Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 USC §112 second paragraph.

Claims 19-21 and 28-30 were rejected based on 35 U.S.C. §102(b) as being anticipated

Claims 19-21 and 28-30 are rejected under 35 U.S.C. §102(b) as being anticipated by Simmons *et al.*, Muerhoff *et al.*, and Scarselli *et al.* The Action further states that Simmons *et al.* teach passage of the "GB agent" in tamarins and other primate hosts. The Action also states that Muerhoff *et al.* teach the cloning of the GBV-B from the serum of the GBV-B infected tamarin. The Applicants traverse this rejection and state that none of the prior art references teach or anticipate the present invention.

For a prior art to anticipate, every element of the claimed invention must be identically shown in a single reference. These elements must be arranged as in the claim under review, but

this is not an "ipsissimis verbis" test (*In re Bond*, 910 F2d 831,15 U.S.P.Q.2d 1566,1568 (Fed. Cir. 1990)).

Claim 19 recites "A method of producing a virus comprising: introducing into a host cell a recombinant viral expression construct comprising a polynucleotide encoding a 3' sequence of GBV-B, wherein the polynucleotide comprises 50 contiguous nucleotides from SEQ ID NO:1; and culturing said host cell under conditions permitting production of virus from said construct."

Simmons *et al.* teach a method of using representational difference analysis (RDA) to clone specific nucleotide sequences presented in serum from a tamarin infected with the GB hepatitis agent and demonstrated that they are immunologically distinct from other known viral agents of hepatitis. This publication does not concern a "method of producing a virus" and does not describe either of the recited steps of the claimed invention.

Muerhoff *et al.* teach a method of using PCR-based techniques to clone cDNAs from GBV-A and GBV-B and provide a detail analysis of their genomic organization to that of other positive strand RNA viruses using sequence alignment and structural data in the form of hydropathy plots. It also does not concern a "method of producing a virus" either explicitly or implicitly. There is no teaching of either step of the claimed invention. Furthermore, these authors' characterization of the clones clearly indicate they did not have "polynucleotide encoding a 3' sequence of GBV-B, wherein the polynucleotide comprises 50 contiguous nucleotides from SEQ ID NO:1." Not only is the sequence of SEQ ID NO:1 not disclosed in the Muerhoff paper at all, but they never demonstrate, much less attempt, the production of an infectious virus based on their clones. Thus, there is no reason to believe this reference teaches the claimed method that involves a "polynucleotide encoding a 3' sequence of GBV-B, wherein the polynucleotide comprises 50 contiguous nucleotides from SEQ ID NO:1."

Scarselli *et al.*, teach the assembly of a synthetic gene of the putative NS3 protease domain of GBV-B and characterized its enzymatic activity. It did not concern any significant portion of the viral genome. It does not teach either "introducing into a host cell a recombinant viral expression construct comprising a polynucleotide encoding a 3' sequence of GBV-B," or "culturing said host cell under conditions permitting production of virus from said construct," both of which are required by claim 19. Like the Muerhoff and Simmons papers discussed above, there is no disclosure of the 3' sequence of GVB that is recited in the rejected claims. Therefore, Scarselli cannot anticipate the claimed invention.

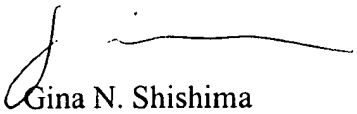
Applicants were the first to identify and provide the "3' terminal sequences of GBV-B wherein the polynucleotide comprises 50 contiguous nucleotides from SEQ ID NO:1", as the claims require. None of the prior references teach such a GBV-B virus. Thus, in light of the aforementioned the Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 USC §102(b).

CONCLUSION

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3081 is respectfully requested.

Respectfully submitted,



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